To:
Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, Maryland 20852

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Comments Pursuant to:
Docket No. 00N-1396
Premarket Notice Concerning Bioengineered Foods

Submitted by:
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Comments:
International Certification Services, Inc. (ICS) is an organic foods certification agency based in North Dakota, USA, doing business worldwide. The program currently does business under the name Farm Verified Organic (FVO) and has done so since 1980. FVO/ICS is accredited by International Organic Accreditation Services, Inc. (IOAS) to the program requirements of the International Federation of Organic Agriculture Movements (IFOAM) Accreditation Program. FVO/ICS also holds accreditation by USDA for compliance under ISO Guide 65 requirements. The company intends to be included in the first of round of certifying agents accredited by USDA under the new National Organic Program (NOP), under the direct auspices of the company's parent name ICS, as a distinct organic certification service specific to the new NOP rules. FVO/ICS will also continue to offer certification under the FVO logo.

Herewith FVO/ICS addresses its comments to FDA's proposed rules in 21 CFR parts 192 and 592 together. Our comments for each section are essentially the same. Our reference to part 192 also speaks to our comments on the corresponding section in part 592. While we shall address our comments in the context of human consumption, we have the same opinion as regards impact of bioengineered foods on animals and the general environment.

All statements set in quotation marks are passages taken directly from Docket No. 00N-1396. We present our comments under several key points, as follows:

I. Concerning FDA's duties and responsibilities as a federal agency:

In general, both the Preamble and the Proposed Rules as presented in Docket 00N-1396 do not reflect that FDA is fulfilling its duties and responsibilities as outlined in the US Code.

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US Code Title 21 – Food and Drugs Chapter 9 – Federal Food, Drug, and Cosmetic Act Subchapter IX – Miscellaneous Sec.393 states FDA's mission and responsibilities regarding the introduction of foods to the mainstream consumer supply. This section of the US Code clearly states that FDA shall undertake measures to ensure the safety of foods provided to consumers, and that such evaluations as to safety will be made through appropriate review, conducted by a broad range of participants – experts in science, medicine, and public health, and in cooperation with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products.

Furthermore, this section of the US Code goes on to state that FDA shall make its processes for arriving at its conclusions increasingly transparent over time, indicating the responsibility of FDA to respond to questions regarding its determinations.

We interpret the proposed rule in Docket 00N-1396 as not fulfilling these above-mentioned basic charges. The proposed rules do not suggest that there will be independent or objective scientific review of the data presented in the Premarket Bioengineering Notices (PBN's). Nor do the proposed rules allow for adequate input from consumers, or an easy way for concerned parties to access information regarding the release of bioengineered products into the environment and mainstream food supply, *prior to their being released.*

FVO/ICS has already responded to Docket 00D-1598 (Draft Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Developed Using Bioengineering; Availability), in which we stated our concerns over what we believe to be FDA's poor regulation of bioengineered materials as regards their labeling and identification. That docket and the current one being discussed obviously go hand in hand, so we respectfully request that FDA refer to our response therein for further background.

It is obvious from the two dockets that FDA favors the release and marketing of bioengineered materials. We shall describe below, from the discussion presented in Docket 00N-1396, how we perceive that FDA has a biased rather than an objective stance toward bioengineering. A bias in favor of bioengineered goods confers an unfair advantage to bioengineering companies, while putting at risk the health concerns of consumers, their right to choose, and the viability of certified organic production. We point out here that the United States government has already approved regulations for organic production via its National Organic Program, and we expect that FDA will do its part to cooperate with USDA to ensure that that program is indeed viable and enforceable. We also note that a prohibition on bioengineering has already been incorporated by Codex Alimentarius in organic production guidelines.

We request to know the full balance of opinions from qualified scientists received by FDA to date, from within its own department, other governmental departments, and the private sector, which attest to precautions warranted and/or food or environmental safety concerns had regarding bioengineered organisms and products. We believe that FDA received a variety of such opinions. In fact we have received news of allegations over the

past year that FDA has suppressed opinions and concerns against the release of bioengineered materials into the mainstream. We request that FDA respond to such allegations. If such opinions were repressed, we want to know why.

FDA states that, "developers of new foods have a responsibility to ensure that the foods they offer to consumers are safe and in compliance with all requirements of the act." We feel this statement reflects FDA's failure to assume its full responsibilities when evaluating bioengineered materials, and that this lack is reflected throughout the preamble and the proposed rule. It is **FDA's** responsibility and duty to the American people to ensure that foods are safe, not the sole responsibility of the product developer; for FDA to place the responsibility on the developer is to abdicate its own responsibility as a government regulatory body.

FDA also goes on to state that, "FDA believes that the food products of rDNA technology are appropriately made subject to greater regulatory scrutiny by FDA in the form of enhanced agency awareness of all such foods intended for commercial distribution." FVO/ICS points out that "enhanced awareness" simply does not and will not suffice as due diligence on FDA's part in its oversight of the entry of bioengineered products into the environment and marketplace. We suggest below procedures that conform to more widely accepted standards for due diligence to ensure that foods are safe; these include a presentation and analysis of data which goes well beyond those of the entities who submit a PBN.

II. Regarding FDA's stated assumptions regarding bioengineered materials:

a. Environmental impact:
FDA states that, "The agency has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environment assessment nor an environmental impact statement is required."

We strongly disagree. How has FDA arrived at this conclusion? There is growing evidence that certain bioengineered crops and microbes can and have had a lasting effect on the environment. While the data obtained thus far only covers the past few years, it is sufficient to warrant careful consideration as to both its immediate and long-term affect on the environment. A few examples illustrate our view:

i) Ladybugs, a widely recognized beneficial insect to farmers and gardeners, are either killed or substantially reduced in their fertility by consumption of aphids that feed on Bt potatoes. Note that a non-target organism has been affected.
ii) Roundup Ready canola has outcrossed via insect transfer of pollen to create weed varieties of the mustard family which are themselves resistance to the herbicide.
iii) The Starlink gene outcrossed so substantially during the 2000 crop year and was commingled during harvest to the point that millions of dollars in marketable goods were lost, both by conventional and organic farmers.

iv) The seed corn supply in the United States for 2001 is pervasively contaminated by at least traces of bioengineered varieties. This makes compliance with the National Organic Program requirements, which categorically exclude bioengineering (especially in seed), extremely difficult if not impossible. FDA's unwillingness to strictly regulate the flow of bioengineered goods will greatly work against the enforcement of another US governmental program.

v) Several bioengineered species, particularly those which include pesticidal action (such as Bt potatoes or corn with the Cry9C gene) have been shown to have alterative effects on soil microbiology. As the soil is a complex system that affects the entire food production chain, the effects imposed upon it by bioengineered organisms needs to be carefully studied.

vi) Some studies have shown that monarch butterflies decrease in reproductivity by their feeding on Bt corn pollen.

While it may not technically be FDA's charge to regulate the environmental impacts of bioengineered organisms and their products, it is imperative that FDA recognize that the quality of the final food products and the methods whereby they are produced are inextricably linked. We encourage FDA to take an interdisciplinary approach to regulating bioengineering, along with EPA and USDA. The nature of this new and unpredictable technology requires that innovative methods to regulate it be also developed. Even if, for example, pesticidal substances are regulated by EPA, it should be incumbent upon FDA and EPA to coordinate research and evaluations, as the alterations made that generate the pesticidal action may have other unintended affects on the food product. Furthermore, such changes in the seed, if poorly regulated by FDA, EPA, USDA, and or other divisions of the US government, will circle back onto the food supply, whether or not this was intended to be the case.

It appears to us that FDA has either not received or chosen to ignore the data available that attest to the environmental affects of bioengineered crops. Since FDA is approving materials which will mostly be introduced into the food supply via their production in the field, it is FDA's responsibility to take those impacts into consideration. FVO/ICS would be glad to furnish data to FDA, if FDA requests it. It is surprising to us that FDA has made the conclusion it has; as presented in the docket, it seems to be proof by blatant assertion.

Furthermore, when an agronomic effect is manifest, this is a sign that changes have gone on in the new organism. Without in-depth study of the new organism, there is no way to properly assess whether or not there are corresponding changes in the food product. Basic tenets of cellular biology tell us that one change within the cell almost certainly causes others; this is part of the organism's constant striving for homeostasis.

Just because it has not yet been discovered what the nutritional differences are in the bioengineered product, does not indicate that there are no changes. Another example:

Roundup Ready soybeans, when consumed by dairy cows, result in milk production that has an altered fat balance compared to cows that eat traditional varieties of soybeans.

Cows treated with rBST have been shown to have elevated levels of Insulin Growth Factor 1 (IGF-1), which in turn has been shown, in elevated levels in the human diet, to increased the likelihood of prostate cancer. Neither of these changes were the intended result of the developer of the bioengineered product, yet they nonetheless are manifest. What other changes exist in the nutritional profile of the milk? What effects will such changes have on human health and nutrition, both in the short and long-term? The developer may not know, because the developer may not have asked such a question. The developer's ostensible concern was agronomic, not nutritional. Indeed, the developer might not wish to ask such questions, if they did not have to go to the expense and time of doing so, especially if such unpredicted changes in the food product would lend credence to the opinion that said product should not be marketed.

The above example illustrates how FDA needs to be aware of both the agronomic properties and the nutritional properties of all bioengineered organisms and the products derived therefrom, as the two are linked, although this might not be obvious if one chose not to investigate.

FDA makes a statement in the preamble which we find rather curious and revealing as to FDA's bias in favor of bioengineered foods: "Bioengineered foods have the potential to offer multiple benefits such as: Improved yield, drought resistance, disease resistance, improved flavor, longer shelf life, increased nutrition, and reduced need for pesticides, among others. Consumers have expressed concern, however, about possible risks that can accompany bioengineered foods. From a public health perspective, the main concerns are allergenicity and toxicity."

We find it interesting to see such a statement from a governmental agency which is supposed to evaluate new products objectively, especially in light of numerous concerns voiced by consumer, environmental, and scientific groups. In light of the examples given above, and the widespread concern about the release of bioengineered organisms and goods into the environment, we want to know what prompts FDA to make such proactive statements. While the positive effects stated by FDA could conceivably occur in some cases, it is our observation to the contrary that such results have generally not yet occurred, and that concerns about the negative impacts of bioengineered species on human health and the environment to date greatly outweigh the hoped-for (and largely unrealized) benefits. The Cartagena Protocol on Biosafety, the labeling requirements imposed in the European Union and Japan, and the growing rejection of bioengineered seed by numerous third-world countries is testament to concerns which FDA seems to be ignoring. What is FDA's rationale for not at including in its discussion the negative effects of bioengineered goods here, while mentioning the hoped-for good effects?

In summary, the concerns are greater than allergenicity and toxicity, even if FDA only wants to assess concerns from within a public health perspective. FDA needs to broaden its perspective on these issues as detailed above.

b. Narrow crosses

It is FDA's assumption that, " Narrow crosses, because they generally are performed between varieties that are themselves used in food or are very closely related to varieties used in food, are unlikely to introduce extraneous DNA that encodes traits that have not been in food before... Therefore, narrow crosses are unlikely to result in unintended changes to foods that raise safety or other regulatory questions."

Again, we disagree, and we provide an example to illustrate our point:

Several years ago a pharmaceutical company engineered a microbe to produce elevated levels of L-tryptophan. The bioengineering technique was a doubling of the L-tryptophan producing gene. The resultant cells produced so much L-tryptophan that the excess was converted into a tryptophan dimer, which turned out to be a potent neurotoxin, the consumption of which left over 1500 persons either dead or permanently paralyzed. Again, this was not an intended effect of the manufacturer.

We stress that FDA does need to receive information about all bioengineered products, be they the result of narrow crosses or not.

One idea which we emphasize that FDA needs to take into consideration when evaluating bioengineering is that the technology itself is extremely powerful, and is qualitatively different from all other breeding methods heretofore available to mankind. The random, inaccurate, and transgenic nature of much of the product development leaves open many questions that were never relevant before. This, coupled with our relatively limited understanding of intracellular interactions, leaves much room for further investigation prior to being able to make sound assessments as to a bioengineered product's safety.

c. *Regarding differences in bioengineered goods compared to their traditional counterparts*

We find FDA's stance regarding the material differences between bioengineered goods and their traditional counterparts to be self-contradictory. FDA makes several statements with which we agree, to the effect that there are likely to be unpredictable outcomes as a result of bioengineering technology, and that it may not be possible to automatically assume that all bioengineered products will be safe for consumers. To excerpt a few such statements from Docket 00N-1396:

- "FDA is aware, however, that rDNA technology continues to evolve and that it is not possible for the agency to anticipate all of the novel scientific and regulatory issues that may arise as the number and types of foods developed using this technology expands."
- "...FDA expects that these techniques are likely to be utilized to an increasingly greater extent by plant breeders and that the products of this technology are likely in some cases to present more complex safety and regulatory issues than seen to date."
- "...In such circumstances, the new substances may not be GRAS and may require regulation as food additives."
- "...rDNA technology can be used to express proteins at higher concentrations than they would otherwise be expressed; these higher concentrations may increase the potential for such proteins to be allergenic."

- "Thus, with rDNA technology, the introduced genetic segment may insert into a genetically active chromosomal location. Such insertion may disrupt or inactivate an important gene or a regulatory sequence that affects the expression of one or several genes, thereby potentially affecting adversely the safety of the food or raising other regulatory issues."
- "...an undesirable substance that is introduced into a bioengineered food, even at a low level, has the potential to adversely affect an animal that eats the food."

The examples mentioned in section IIa and IIb above are real illustrations of how these potential dangers have already been manifested. The lifelong effects of such undesirable or potentially dangerous substances have yet to even be discovered, particularly for those species with a longer lifespan, such as humans and larger mammals.

FDA makes several references to "unintended effects" of bioengineering. How will such unintended effects be discovered, evaluated, and monitored? It is clear that FDA agrees with us that potentially hazardous effects may result in bioengineered products. If FDA is to fulfill its responsibility to the American public as regards food safety, then there needs to be specific mechanisms and procedures in places to ensure that analysis and review of the proposed bioengineered products is rigorous and that the products are indeed safe. Below, we recommend several such procedural mechanisms.

However, FDA also states in several cases that they have no reason to believe that bioengineered foods are different enough to warrant significant questions as to their safety, nor any special labeling. In light of the already existent and growing evidence from field and laboratory research which has been conducted to the contrary, we want to know on what basis FDA makes its conclusion – especially given the other statements by FDA quoted above.

FDA states that, "...many modifications will result in a food that does not contain an unapproved food additive, does not contain an unexpected allergen, and does not differ significantly in its composition compared with its traditional counterpart or otherwise require special labeling."

FDA needs to define what a significant difference is, and how that will be evaluated. We believe this to be a difficult task, as the changes that will be manifest in the bioengineered food may not always be readily obvious, especially without exhaustive research, analysis, and review of the goods in question.

FDA indicates that, "Under the regulation, a 'modified substance' would include a substance that is present in the bioengineered food at an increased level relative to comparable food." What defines an "increased level"? How will FDA be able to make this determination as to whether or not a bioengineered food contains a modified substance? We believe that formalized criteria and protocols need to be established by FDA, in concert with independent scientific bodies, to assess whether or not research conclusively shows that the bioengineered material proposed for release has or does not have modified substances. We foresee this as being a combination of rigorous and

detailed laboratory analyses coupled with extremely highly controlled laboratory and then *in vivo* trials; we would gladly offer more detailed suggestions to FDA. If modified substances are present, then further studies are needed to assess their impact. In the end, if such determinations cannot be made beyond all reasonable doubts, then said goods should not be marketed.

FDA continues later by stating that, "...It is impracticable for FDA to either anticipate all classes of substances that could be introduced into food or provide specific guidance about each of those classes of substances."

While we do acknowledge that the full evaluation of bioengineered materials is difficult to perform, we do not agree with FDA that this is ground for not performing extremely diligent review prior to granting permission to release into the food production mainstream. The known examples of negative effects of bioengineered foods should give FDA substantial reason to employ a precautionary approach with such goods. To cut reviews short so that products can make it to market faster or more easily is an abdication of FDA's responsibility.

As a side note, we point out that part of the regulatory challenge that arises here originates with the original judicial decision that permitted the patenting of life in the first place. Bioengineering may ultimately provide some valuable benefits to mankind, but the pitfalls are obvious. Were bioengineering research conducted in a socially responsible manner, this might be an acceptable approach to learning to use this technology. However, the market incentive of many bioengineering companies short-circuits adequate research on their goods, as those companies prefer to see a premature profit return on their investment. Products have been released into the environment in a poorly controlled and poorly understood manner, and the consequences are difficult to reverse – and may be impossible to reverse if things are allowed to continue as they have. (The Starlink debacle is a clear case in point, but it is only one of others which already exist.)

Nonetheless, if products cannot be reasonably assured to be safe, both in an environmental and food context, they should not be allowed to be released. The market incentive of certain companies should not be able to influence such decisions by FDA; FDA's primary responsibility is as a service to the American people, not as a facilitator of big business interests.

As a final example for this section of our comments, we quote FDA in the preamble of the docket: "Intended changes to the composition or characteristics of the food also could raise safety questions about the food. For example, it is possible that a developer could modify corn so that the corn becomes a significant dietary source of the nutrient folic acid. Folic acid is used to fortify many foods, including breakfast cereals, because of the relationship between consumption of folic acid and a reduced risk of neural tube defects (21 CFR 101.79). However, excess folic acid in the diet can mask the signs of vitamin B12 deficiency. Thus, an increased level of folic acid in a food such as corn, which is commonly used in breakfast cereals, could raise safety or other regulatory issues." It seems here to us that while FDA rightly points out a level of complexity that needs to be

considered, FDA throughout much of the docket fails to acknowledge how much more of these types of complexities exist in cellular and other biological systems which we simply do not yet know about. To only take into consideration the relatively few facts we know about, and to basically ignore the rest because "there is no scientific evidence yet to indicate a problem" is simply bad science.

In summary, we disagree with FDA's proposed submission requirements as given in the docket. We reiterate that many of the negative results of bioengineered foods, as mentioned in this comment and in our response to Docket 00D-1598, were not intentional or direct effects of the ostensible objective of the bioengineering performed on those organisms. It seems altogether likely that similar negative effects will arise in the future, should releases continue to be allowed by FDA without more careful reviews.

We recommend below ways to help ensure that review of bioengineered goods is more fair and thorough.

d. Regarding already-approved and marketed bioengineered goods, and whether or not they should be subject to new review:

Due to the evidence thus far obtained that some bioengineered materials already on the market are having negative effects, both environmentally and nutritionally, we disagree with FDA that those products already approved or pending approval need not be subject to the current proposed regulation. Indeed, their manifested negative effects rather beg that they be reviewed again, more carefully, to determine whether or not their continued release should be allowed. Even if not all bioengineered products have specifically evidenced themselves as having unwanted effects, the fact that several already have been shown as such is indicative that the regulatory and review process prior to their release was inadequate. This calls into question the safety of all goods released under those protocols, and further review is therefore warranted.

III. Regarding FDA's proposed process of Premarket Bioengineering Notices as a means to regulate bioengineered materials:

FVO/ICS emphasizes to FDA that the proposed regulation requiring a Premarket Bioengineering Notice (PBN) from the developer or marketer of a bioengineered product should be only one minor step of several more steps involved in achieving FDA approval for such goods. Instead, the PBN, as proposed in Docket 00N-1396, plays the major role in the gaining of permission to release such goods into the food stream.

In general, we interpret the proposed rule as extremely lax, almost completely passive on FDA's part. FDA states that, "As a practical matter, the proposed regulation will give flexibility to its producers while providing the agency with information concerning the nature of bioengineered foods." True enough, the proposed rule will provide perhaps undue flexibility to marketers of bioengineered goods. However, we strongly disagree that the amount and quality of information required by the proposed rule will be adequate for FDA to fulfill its responsibility to the public.

We suggest that the PBN be only the first step in the approval process. As such, to even refer to it as a "Premarket Notice" is, we feel, a misnomer, and we request FDA change the name. Such notice should be an *Application to Market* bioengineered materials, or a *Request for Review* of proposed bioengineered materials, or similar. To call it a premarket notice implies that the material is pretty much destined for market, before FDA has even had a chance to look at it – again, we feel this is reflective of FDA's bias toward moving such products into the mainstream without due diligence on its part.

FVO/ICS requests that the process be amended to contain five distinct phases. These phases parallel other governmental systems for review of materials requested for use in food production systems. One such process with which FVO/ICS is familiar is the review of materials for use in organic production, as items to amended to the National List of materials for such use under the National Organic Program. If that process is mandated for materials which have, for the very large part, far less reaching effects than do bioengineered goods, it seems entirely reasonable that at least as diligent a process be followed for bioengineered goods.

The process is, in summary:
a. Application or petition for allowance of the new material
b. Agency review of the application
c. Peer review of both the data presented by the notifier and the agency evaluations thereof
d. Public comment
e. Final decision

We note that the proposed rule includes a form of only the first two of the processes mentioned above. Below, we critique FDA's proposal, and add suggestions thereafter as to how to complete the process for the remaining steps.

a. Submission of the PBN, and the presubmission consultation:
In the proposed rule, FDA relies far too heavily on the notifier for information. We have the following questions and comments:

i. Proposed section 192.10(f)(3)(v) and (vii) request information from the notifier that cannot be adequately supplied by the notifier alone. The notifier has, even in the most ideal cases, a conflict of interest with its own product, in that the interpretation given for the requested bioengineered material cannot and will not be subjective; to wit, they want approval for their product. We do not see how FDA has addressed the issue of conflict of interest in this proposed rule, and we want to know how that will be handled.

Subsection (v) requests submission of information about "expected significant changes" in the food. What about unexpected changes? How will FDA evaluate these? What criteria will be assigned to a review of such characteristics, to be sure that adequate consideration and analysis of the goods have been performed? Subsection (vii) asks for "a description of any applications or uses that are not suitable for the bioengineered food." If history is a teacher, we can be assured that the answers by the notifier to such a question will not be

adequate to protect the public and the environment, as evidenced by the many examples cited previously in these comments. How can FDA rely solely on such presentations from the notifier? On what basis has FDA made the conclusion that such presentations will be adequate?

ii. In the preamble to the proposed rule, FDA states, "FDA also is proposing that a notifier state that to the best of the notifier's knowledge, the PBN is a representative and balanced submission that includes information, unfavorable as well as favorable, pertinent to the evaluation of the safety, nutritional, or other regulatory issues that may be associated with the bioengineered food (proposed §192.25(a)(2))." We find this statement odd, in that a self-assessment by the notifier of the adequacy of their proposal seems to completely short-circuit an adequate review process by FDA. It should be FDA's determination as to whether or not a proposal is balanced. Such determinations can only be made after objective evaluations of the data presented have been undertaken; the notifier alone cannot do this. What criteria will FDA use to assess whether a proposal really is balanced? Furthermore we do not see that section 192.25(a)(2) even requires this at the time of submission of the notice. 192.25(a)(2) states, "You agree to make relevant data or other information that are not included in your PBN available to FDA upon request, either while FDA is evaluating your PBN or for cause." This does not even require all data be submitted with the notice, only that it be available. FDA should require all data obtained; then FDA can have a better chance to assess whether or not the presentation and research on the proposed bioengineered food is balanced. How can FDA feel confident that a notifier could choose which data to present to FDA upon submission of the notice, and choose to not submit other pieces? Even though section 192.25(a)(5) calls for a representative and balanced presentation, this assessment is again being made by the presenter; it is a form of "self-certification," a process which does not attest to any real oversight. This falls short of what would seem to be the minimum requirements of an adequate review. Only by full submission to FDA of all data obtained by the notifier can such assessments as to a balanced presentation have any worth at all.

If FDA proceeds in the mode that it proposes, it seems far more likely that problems will arise after bioengineered foods have been marketed. This makes it more likely that we shall learn about potential problems with bioengineered foods only after problems have become manifest in the public and/or the environment. Starlink is a classic example. How many more people will go into anaphylaxis from eating this material? It is FDA's duty to undertake all possible steps to ensure that problems are avoided before they become obvious through tragedy; how does FDA justify its current approach?

iii. FDA states that, "Consistent with the 1992 policy, the 1996 procedures, and FDA's experience under the 1996 procedures, FDA is proposing that a notifier provide data or information comparing the composition and characteristics of the bioengineered food to those of comparable food(s), with emphasis on changes in the levels of significant nutrients and naturally occurring toxicants and antinutrients (proposed § 192.25(g)(3)(i) and (g)(3)(ii))." First of all, FVO/ICS points out again that in light of evidence gained since 1996 with bioengineered

foods, FDA needs to revise its thinking on how to regulate products of bioengineering. Secondly, on what basis will FDA be able to assess whether or not the data presented on the issues mentioned here is complete or thorough? What rigor of analysis is required or will be required?

iv. Section 192.25(g)(4) requires the notifier submit "Any other information relevant to the safety, nutrition, or other assessment of the bioengineered food." Who decides what is relevant? If this is left up to the notifier, FDA has shortchanged itself and the public of a diligent review.

v. "FDA also is proposing that a notifier inform FDA as to whether the bioengineered food is or has been the subject of review by any foreign government and, if so, describe the status of that review (proposed §192.25(c)(3))." It is the opinion of FVO/ICS that the responsibility for such verification should not rest with the notifier, but rather that it should rest with FDA. Otherwise, how will FDA assess that the search for such information as performed by the notifier was diligent and complete? If such research by FDA requires extra labor and time, that cost should be incurred by the notifier. Also, does this search include searches for relevant reviews for "similar foods," as discussed by FDA in this docket? We request that FDA better define "similar food" as used in the docket. FVO/ICS believes that all new submissions need to be reviewed by FDA, and that "similarity" may quite likely be an oversimplification, considering that the effects of bioengineering technology and its current lack of exactness that still exists with it. (See the comments above in IIb under "Narrow Crosses" for related discussion.)

vi. In response to FDA's inquiry as to whether the rule should include a requirement that a PBN include methods by which the food could be detected, we heartily agree that such a requirement be included. Such required methods should contain all possible information to enable technically proficient laboratories (governmental and non-governmental) to use them for detection. This requirement should cover raw agricultural commodities as well as processed goods. This is one assurance that FDA can and needs to give to the public in the event that a product recall or other investigation is needed.

vii. FDA proposes in section 192.25(f)(5) that the notifier be required to include "a discussion of data or other information relevant to other safety issues that may be associated with the substances introduced into, or modified in, the food." To what other types of safety issues is FDA referring? FVO/ICS believes there are a variety of related safety issues, as regards agricultural operations, livestock operations, and general environmental impact, not to mention the food safety issues. We ask that FDA be more specific here.

viii. There is much reference to the "Presubmission Consultation" in the docket. While we do not oppose FDA's cooperation with product developers and marketers, we do feel that this part of the process as currently presented lacks transparency. These consultations need to be formalized in structure by FDA, to ensure that an equal process is guaranteed to all potential participants. What guidelines, criteria, and operating protocols will be employed for these sessions? What specific points will be required in the consultations? How will the content

of the consultations be documented? We request that such detail be provided in section 192.10(a) of the proposed rule.

ix. We have some concerns that transparency in the review process may be further compromised by claims of confidentiality and exemption from the Freedom of Information Act. While we respect the terms of the FOIA, we request that FDA publish some more detailed specific types of information which would be withheld from public access, and more detail on what "applicable criteria for exemption" are as relates to bioengineered foods.

Of even greater concern to us is that FDA considers the possibility that existence of PBN itself might be confidential. Under what circumstances would this be possible? Does this mean that there is the possibility that a marketer could have a bioengineered product approved for release into the food stream or environment without the public even knowing about it? We strongly object to such a possibility. FDA must make known the existence of all PBN's.

b. Notification by FDA

For a number of reasons stated throughout these comments (both above and below), FVO/ICS believes that 120 days is an insufficient amount of time necessary to perform acceptable reviews of bioengineered materials. It may be possible that FDA can issue a decision in 120 days or less, but we object to the idea that such reviews should have any time limit at all. We acknowledge that FDA has kept the door open to the possibility that approval may take longer, but nonetheless, the way the proposed rule is couched, the impression is given to the notifiers and the public at large that 120 days connotes almost a type of *fait accompli* that such defined timelines are appropriate. We therefore request that FDA restructure its proposed rule to not specify any time limit. Concomitant with this is the revision of the concept of a "premarket notice," as discussed above, to that of an *application for approval* or similar wording.

FDA goes on to state that it expects that the list of filed PBN's will be updated approximately monthly. We encourage such updating on at least this frequent a basis.

Section 192.40(e) is only sufficient as stated, if additional steps in a review process as outlined below are undertaken. Peer review and public comments are needed for diligence to the subject. FDA should therefore plan to make public more of the background on its final decisions.

We are also confused by certain statements made by FDA in the preamble relative to "developers who have not chosen to notify FDA." Isn't the proposed rule applicable to all developers of bioengineered foods? Under what circumstances would a developer/marketer not have to notify FDA? Any such situations seem completely counter to FDA's stated intention of the proposed rule, and we strongly object to the possibility of their allowance. Similarly, earlier in the preamble FDA states, "If a notifier initiates commercial distribution of a bioengineered food after being informed that the applicable notice is not adequate, FDA will carefully and completely review the legal status of the applicable food and will use all available options to ensure that the food is fully in compliance with all provisions of the act. In particular, in such circumstances, the

agency fully intends to bring to bear the complete range of its authorities and resources, including its authority under section 704 of the act (21 U.S.C. 374) to conduct inspections and investigations, collect samples, and perform analyses, as well as its authority under sections 705 and 903 of the act (21 U.S.C. 375 and 393) to engage in publicity and public education. When the agency concludes through the application of these resources that a food is adulterated, misbranded, or otherwise not in full compliance with the act, FDA will utilize the act's legal sanctions, as appropriate, including in rem seizure of violative foods and injunction proceedings against, or criminal prosecution of, those responsible for distributing such foods." While we appreciate the measures FDA describes in reaction to such acts by notifiers, we do not agree that the measures suggested by FDA are quite enough. Rather, any violation of the rules, particularly unauthorized marketing and/or release of bioengineered materials, should be met with clear and extremely severe penalties, including all costs associated with removing said goods from the food stream regardless of their deemed violative character, ensuring that seeds stocks thenceforth are not contaminated by the material, and the prohibition of an entity from developing (not just marketing) any further bioengineered materials for a significant length of time. Such penalties are often given in cases of serious violations; one analogous case might be the fraudulent marketing of goods as certified organic, which meets with a ban by imposed USDA on any activities in the organic sector for five years.

c. Peer Review

For reasons we cannot understand, it appears that FDA has completely ignored the vital step of peer review. Objective, independent scientific evaluation of the data presented by the notifiers, as well as FDA's interpretation of that data is needed in order to have enough confidence in the rigor of the review process. Especially when considering a science as open-ended as bioengineering, to not subject all potential releases of bioengineered materials into the food stream is wholly irresponsible. We want to know why FDA has not included peer review as part of its process.

In short, all of the data presented to FDA by the notifier, and then FDA's response to and/or evaluation of said data, including conclusions drawn by FDA, should be submitted to a qualified panel of scientists, which can then assess whether or not the proposal and review are balanced, scientifically rigorous, and complete enough to draw a conclusion in favor of approval of the bioengineered goods by FDA. We request that FDA consider the existence of such a peer review panel, propose how said panel would be constituted, and formulate rules of action by the panel members. The charge of said panel should be to consider all potential impacts of the bioengineered materials, from food safety, environmental, and social perspectives, and as such, should probably be an interdisciplinary panel formed with the cooperation of FDA, EPA, and USDA. All peer reviews should be public information.

There are many points already mentioned in this review that are relevant to peer review. We mention here additional areas referenced in Docket No. 00N-1396 where peer review finds relevance:

- "In June 1996, FDA provided guidance to industry on procedures for these consultations (the 1996 procedures (Ref. 5)).4 Under that process, a developer who

intends to commercialize a bioengineered food meets with the agency to identify and discuss relevant safety, nutritional, or other regulatory issues regarding the bioengineered food prior to marketing it." FVO/ICS believes that said guidelines set by FDA should have been subject to peer review for soundness prior to their implementation. If there was peer review, where can the results of that review be found?

- "FDA is proposing that a PBN include data or information about the method of development (proposed § 192.25(d)). Specifically, FDA is proposing that the data or information that a notifier provides regarding the method of development include:... (3) characterization of the introduced genetic material, including the number of insertion sites, the number of gene copies inserted at each site, and information on DNA organization within the inserts; and information on potential reading frames that could express unintended proteins in the transformed plant (proposed § 192.25(d)(3)); and (4) data or information related to the inheritance and genetic stability of the introduced genetic material (proposed § 192.25(d)(4))." These are pieces of information which warrant rigorous review, to ensure that point (3) is correctly stated, and that point (4) is reasonably evaluated. In reference to this latter point, studies have shown that bioengineering technology sometimes does result in less stable genomes than traditional varieties, as and such, can result in more frequent mutations, the effects of which are unpredictable, and should therefore be regarded with caution.
- "FDA is proposing that a notifier include either: (1) An estimate of dietary exposure to substances introduced into, or modified in, the food (proposed § 192.25(f)(3)(i)); or (2) a statement that explains the basis for the notifier's conclusion that an estimate of dietary exposure to these substances is not needed to support safety (proposed §192.25(f)(3)(ii))." How does FDA rationalize that assessment of such factors would be valid, if these were only being substantiated by the notifier? Again, the notifier has an unavoidable conflict of interest, and their claims need to be supported by non-interested views in order for them to be acceptable as scientifically valid.
- "FDA is proposing to require that a notifier provide a narrative that explains the basis for the notifier's view that the bioengineered food is as safe as comparable food and that the bioengineered food is otherwise in compliance with all applicable requirements of the act (proposed § 192.25(g)(5)). The narrative would provide an integrated discussion of the data and information submitted in a PBN. FDA is proposing this requirement because the notifier has the responsibility for determining that the intended use of the bioengineered food is as safe as comparable food and is otherwise lawful. Absent an integrated discussion of the underlying data and information, the basis for the notifier's conclusion about the legal status of the bioengineered food may not be apparent." We do not understand how FDA feels that such a narrative, as presented by the notifier, is sufficient. Furthermore, we do not agree with FDA that, "the notifier has the responsibility for determining that the intended use of the bioengineered food is as safe as comparable food and is otherwise lawful." This must be the responsibility of FDA. To pass the responsibility to the notifier is indicative of FDA's willingness to abdicate its responsibility. Moreover, our exposure to such narratives by developers of bioengineered materials clearly falls short of scientific soundness. While often having the appearance of rigor to the uneducated or the layperson, many of the presentations offered by those companies

only appear to have credence if basic tenets of cellular biology and evolutionary theory are ignored. Granted, it is understandable how the layperson might not detect such shortcomings and therefore feel that the developer has "done its homework," but we would only feel comfortable with such narratives if they were scrutinized by qualified non-interested scientific professionals.

- FDA's responses to the notifier regarding the status of the PBN should also be made available to peer review, to afford FDA constructive feedback on its own work.
- "... it is also important to know whether a protein from a traditionally nonfood source has characteristics associated with allergenic proteins." Peer review is needed here to help ensure that relevant research has been adequately considered.
- "The submission of a narrative of the developer's reasons for concluding that the bioengineered food is as safe as comparable food and its justification of the choice of comparable foods by the notifier will aid in ensuring that all potential safety issues have been considered." We reiterate that the notifier's opinion is simply not enough. Furthermore, the narrative as suggested here addresses safety issues, which we presume to mean food safety issues, and does not take into account the necessary larger picture of environmental impact. A peer review should be charged with evaluating the complete picture.

d. Public Comment

Considering the widespread concern in the public at large, as well as in the scientific community regarding bioengineered foods, FVO/ICS argues that a period of public comment is essential to serving all facets of the American public in a fair and rigorous process. Just as in the case with the addition of materials to the National List of the National Organic program, all proposed approvals of bioengineered goods should be subject to a public comment period, during which all interested parties can offer feedback to FDA. The notice of request for public comment should be published in the Federal Register, and should include information from the submitter of the PBN, FDA, and the peer review assessment. Such a process accords with approval of other less controversial materials, so we see no reason that this should not apply to bioengineered materials. We want to know why FDA has not opted to include this as part of the approval process. Expediency of approval is not a valid justification.

e. Final Decision

Only after all public comment has been evaluated, should FDA issue a decision on the bioengineered material. We also request that FDA consider, given the early stage of mankind's knowledge regarding bioengineered organisms and foods, that if approval is granted, that it be for a limited time period only, not more than a few years, and that a renewal application be required. This will allow for follow-up assessment of the bioengineered goods, as well as a greater ability to regulate their flow should the need arise to do so.

IV. Additional Considerations

a. Economic impacts on organic producers

The uncontrolled flow of bioengineered goods in the agricultural and food manufacturing sectors has already had damaging effects on organic producers and conventional

producers of traditional varieties of certain crops. Bioengineering as currently practiced, and as seemingly proposed by FDA to continue in poorly regulated manner, will adversely affect organic farmland, organic food products, and organic producers, as well as their conventional non-bioengineered counterparts. These effects are and will be manifest in the form of genetic pollution of land, seed stocks, raw agricultural commodities, and processed food products. This will in turn adversely affect the economic viability of numerous farmers and food workers who participate in the burgeoning organic sector. How will FDA protect organic producers from the negative effects of bioengineering? USDA has already approved a National Organic program to promote organic production. For FDA to allow bioengineered goods to flow into the food stream in a poorly regulated fashion is a *de facto* favoring of bioengineered foods over organic. Bioengineering also has the potential to favor large farms over small farms, due to seed availability, differing agronomic techniques involved with bioengineered or traditional varieties, and other socioeconomic factors.

b. Labeling

Please refer to FVO/ICS' response to Docket 00D-1598 for a full discussion of labeling of bioengineered goods. We note in Docket 00N-1396 that FDA states that a bioengineered food would require distinctive labeling if it was substantially lower in certain nutrients. How is this determined? Again, we regard peer review as a fair approach. Roundup Ready soybeans have been shown to be substantially lower in phytoestrogens; does this not constitute a need for specific labeling? While we acknowledge that a requirement of special labeling may be cumbersome for the product developers and marketers, we in no way see this as adequate reason to overlook the need for it.

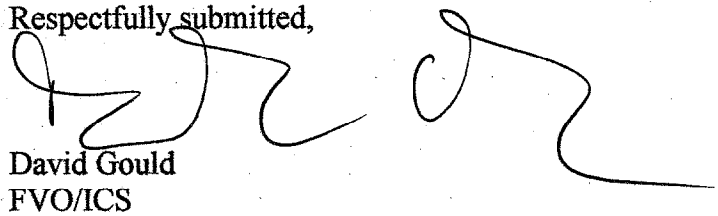
c. Laboratory Costs

FDA requests comments on feasibility and costs associated with laboratory analyses related to bioengineered foods. FVO/ICS is not a laboratory, but we are aware of several competent laboratories that perform such analyses, and FDA should be able to obtain cost estimates from them without difficulty.

d. Economic burden on FDA and notifiers

From all of FVO/ICS' comments given in this response to Docket 00N-1396, we conclude that FDA's estimates for administrative and economic burdens, both of FDA itself and the notifiers, need substantial reconsideration and revision. Only when a proper regulatory scheme is designed can a reasonable analysis of these factors be generated. We believe that the product developer and/or marketer must assume a much greater burden for the costs of reviewing and approving bioengineered materials. FDA will have to do more work as well, but those who are developing such products should incur those costs, as they are the ones who stand to benefit from them. Until the technology becomes much better understood, and regulation thereof is much more rigorously controlled, the evidence obtained overwhelmingly supports the conclusion that those companies are the only ones who will benefit, and that the public at large and the environment will suffer.

Respectfully submitted,



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